

In the Claims:

Please amend claim 8 and add new claims 25 and 26. The following listing of claims will replace all prior versions, and listings, of claims in the application.

1. (original) A substrate having micromachined surface structures provided thereon, wherein said micromachined surface structures comprise nanotopographic features superimposed thereon, the nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired subassemblies within said micromachined surface structures.
2. (original) The substrate as recited in claim 1, wherein one or more micromachined surface structures defines the walls and floor of a channel.
3. (original) A substrate as recited in claim 1, wherein the nanotopographic features facilitate adhesion of one or more cell types.
4. (original) A substrate as recited in claim 2, wherein the nanotopographic features are oriented to preferentially adhere one or more cell types to a desired location on the substrate.
5. (original) A substrate as recited in claim 1, wherein the nanotopographic features are oriented to laterally align one or more cell types.

6. (original) A substrate as recited in claim 1, wherein the nanotopographic features are oriented to form a grid.

7. (original) A substrate as recited in claim 1, wherein the nanotopographic features are generated by a lithographic technique.

8. (currently amended) A substrate as recited in claim 1, wherein the cell types are selected from the group consisting of endothelial cells, smooth or skeletal muscle cells, myocytes, cardiac cells, fibroblasts, chondrocytes, adipocytes, fibromyoblasts, ductile cells, skin cells, hepatocytes, kidney cells, pancreatic islet cells, intestinal cells, osteoblasts, hematopoietic cells and stem cells.

9. (withdrawn) A method of organizing cells on a substrate for use in engineering tissue, said method comprising the steps of: a) generating a micromachined surface structures; and b) superimposing nanotopographic features on the micromachined surface structures in such a manner so as to organize multiple cell types into desired subassemblies for use in constructing engineered tissue.

10. (withdrawn) The method according to claim 9, wherein the micromachined surface structure defines the walls and floor of a channel.

11. (withdrawn) A method according to claim 9, wherein the step of superimposing nanotopographic features includes arranging the nanotopographic features in predefined locations on the substrate.

12. (withdrawn) A method according to claim 9, wherein the step of superimposing nanotopographic features includes orienting the nanotopographic features to preferentially adhere one or more cell types to a desired location on the substrate.

13. (original) A tissue engineered system comprising one or more layers, wherein each layer includes micromachined surface structures having nanotopographic features superimposed thereon, the nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired subassemblies within said micromachined surface structures.

14. (original) The system according to claim 13, wherein a semi-permeable membrane is positioned between the layers.

15. (original) The system of claim 13, wherein one or more micromachined surface structures defines the walls and floor of a channel.

16. (original) The system according to claim 15, wherein the channels are divided longitudinally into two compartments by a centrally positioned membrane, and wherein each compartment comprises a different cell type.

17. (original) The system according to claim 13, further comprising a pumping means for circulating fluid through the system.

18. (original) The system according to claim 13, further comprising nutrient supply and excretion removal lines in fluid communication with the system.

19. (original) The system according to claim 13, wherein the nanotopographic features facilitate adhesion of one or more cell types.

20. (original) The system according to claim 19, wherein the nanotopographic features are oriented to preferentially adhere one or more cell types to a desired location on a layer.

21. (original) The system according to claim 13, wherein the nanotopographic features are oriented to laterally align one or more cell types.

22. (original) The system according to claim 13, wherein the nanotopographic features are oriented to form a grid.

23. (original) The system according to claim 13, wherein the nanotopographic features are generated by a lithographic technique.

24. (original) The system according to claim 13, wherein the cell types are selected from the group consisting of endothelial cells, smooth or skeletal muscle cells, myocytes, cardiac cells, fibroblasts, chondrocytes, adipocytes, fibromyoblasts, ductile cells, skin cells, hepatocytes, kidney cells, pancreatic islet cells, intestinal cells, osteoblasts, hematopoietic cells and stem cells.

25. (new) A substrate having micromachined surface structures provided thereon, wherein said micromachined surface structures comprise nanotopographic features superimposed thereon, the nanotopographic features having a first portion configured to select a first cell type and a second portion configured to select a second cell type so as to organize the first and second cell types into desired subassemblies within said micromachined surface structures when a population of multiple cell types are introduced onto the surface.

26. (new) An apparatus capable of supplementing or replacing at least one organ function comprising multiple layers of tissue lamina stacked and fastened together, wherein each layer of tissue lamina comprises:

a first polymer scaffold configured with a plurality of branched microchannels and having endothelial cells seeded within the branched microchannels to form a vasculature system;

a second polymer scaffold having parenchymal cells within the scaffold to form a parenchymal tissue; and

a semi-permeable membrane disposed between the first and second polymer scaffolds, the semi-permeable membrane configured to allow exchange of oxygen, nutrients and waste between fluid circulating in the vasculature system of the first polymer scaffold and the parenchymal tissue present in the second polymer scaffold;

wherein the first polymer scaffold and the second polymer scaffold are fastened together about the semi-permeable membrane, and

wherein said plurality of branched microchannels or said second polymer scaffold comprise nanotopographic features, the nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired subassemblies within said plurality of branched microchannels of the vascular compartment or said second polymer scaffold.